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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/750,021 | 12/29/2000 | Hans-Georg Frank | P66238US0 | 6410 |

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JACOBSON HOLMAN PLLC
400 SEVENTH STREET N.W.
SUITE 600
WASHINGTON, DC 20004

| EXAMINER | |
|---|---|
| BLANCHARD, DAVID J | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1642 | |

DATE MAILED: 10/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/750,021 | FRANK ET AL. | |
| | Examiner | Art Unit | |
| | David J Blanchard | 1642 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *27 July 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *20-27* is/are pending in the application.

4a) Of the above claim(s) *24-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/10/02; 5/27/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

1. Claims 1-19 have been canceled.

Claims 20-27 have been added.

2. Newly submitted claims 24-27 directed to inventions that are independent or distinct from the invention originally claimed for the following reasons: Claims 24-26 are drawn to a method of identifying low molecular weight substances mimicking mammal epitopes using antibodies that bind said mammal epitopes, which is the invention of Group IV of the restriction requirement mailed 9/23/2003 and is distinct from the elected invention (Group I; method of making monoclonal antibodies that bind epitopes on the surface of trophoblasts or tumor cells) for reasons set forth therein. Newly added claim 27 is drawn to a method of making anti-idiotypic antibodies, which are distinct from the elected invention because the process as claimed can be used to make other and materially different product (i.e., monoclonal and anti-idiotypic antibodies). In the instant case anti-idiotypic antibodies are materially different from monoclonal antibodies because anti-idiotypic antibodies mimic antigen and bind monoclonal antibodies and can be used to make and/or purify the monoclonal antibodies. Also, monoclonal antibodies can be used to purify antigen and anti-idiotypic antibodies cannot. Further, the method of making anti-idotypic antibodies is classified in class 435, subclass 328 and the elected invention of Group I (method of making monoclonal antibodies) is classified in class 424, subclass 155.1. Therefore, the inventions are distinct due to different method objectives, reagents used, different endpoints and different classification and would require different searches.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 24-27 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

3. Claims 20-23 are pending and under examination. Applicant is reminded that the claims are being examined to the extent that the monoclonal antibodies bind to epitopes on the surface of trophoblasts or tumor cells (elected invention of Group I in the paper filed 10/23/2003 and reaffirmed in the Office Action mailed 1/27/2004; see item #'s 2-4 of the Office Action mailed 1/27/2004).

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. This Office Action contains New Grounds of Rejections.

***Objections/Rejections Withdrawn***

6. The objections to the brief description of the Drawings for not describing parts a and b of Figures 1 and 3 and for Figure 1 not being in English are withdrawn in view of the amendments to the brief description of the drawings and the English translation of Figure 1.

7. The objections of claims 1 and 3 are withdrawn in view of the cancellation of claims 1 and 3.

8. The rejection of claims 2-3 and 7 (parts a-e) under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention are withdrawn in view of the cancellation of the claims.

9. The rejection of claim 2 under 35 U.S.C. 112, first paragraph, because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims is withdrawn in view of the cancellation of claim 2

10. The rejection of claims 1-3 and 7 under 35 U.S.C. 102(e) as being anticipated by Mostov et al is withdrawn in view of the cancellation of the claims and the newly added claims.

11. The rejection of claims 1-3 and 6-7 under 35 U.S.C. 102(a) as being anticipated by Schmitz et al is withdrawn in view of the verified translation of the 119 priority document DE 19964046.7, filed 30 December 1999.

12. The rejection of claims 1-3 and 7 under 35 U.S.C. 102(e) as being anticipated by Michael et al is withdrawn in view of the cancellation of the claims and the newly added claims.

13. The rejection of claims 1-3 and 6-7 under 35 U.S.C. 102(b) as being anticipated by Hoogenboom et al as evidenced by Tendler et al is withdrawn in view of the cancellation of the claims and the newly added claims.

***Response to Arguments***

14. Newly added claims 20-23 are rejected under 35 U.S.C. 103(a) as being obvious over Michael et al in view of Schroit A. J. and Huppertz et al is maintained.

The response filed 7/27/04 has been carefully considered, but is deemed not to be persuasive. The response argues that Huppertz et al is directed to cell-syncytium growth and when cell-syncytium fusion occurs, the blastocyst is already implanted into the placenta and any approach aiming at inhibiting cell-syncytium fusion would interfere with the already existing pregnancy and as such relates to the field of abortion. In contrast the approach of the present claims is the inhibition of the blastocyst and as such relates to the field of contraception. In response to these arguments, Applicant has not provided any evidence that the phosphatidylserine (PS) flip does not occur prior to or during syncytial cell-cell fusion of trophoblasts (i.e., formation of the syncytium). As evidenced by Applicant's specification at page 9 when the leading cell population of the blastocyst, i.e., the trophoblast, penetrates the uterine epithelium, the cells of the trophoblast fuse to a syncytial aggregate (a process known as trophoblastic synctiogenesis) and this process of trophoblastic synctiogenesis is triggered by signal epitopes of which it is only known to date that a flip of phosphatidylserine to the exterior of the plasma membrane is involved in their generation. Consistent with applicants specification Huppertz et al teach that in vitro experiments with choriocarcinoma and primary trophoblast cells have shown that this phosphatidylserine flip is involved in syncytial fusion and that blockage of phosphatidylserine by antibodies hinders syncytium formation (see page 504, left column) and as evidenced by Potgens et al

(Placenta, 23 Supplement A, Trophoblast Research, 16, S107-S113, 2002) syncytium formation is the direct result of primary trophoblast cell-cell fusion (see Figure 1, left side). Therefore, in contrast to Applicant's argument Huppertz et al does teach that phosphatidylserine antibodies inhibit syncytium formation or syncytial cell-cell fusion of trophoblasts as recited in the instant claims. Further, Huppertz et al teach epitopes (i.e., PS/proteolipid) which are exposed by a conformational change (PS flip) upon ligand binding (i.e., FasL; see Figure 1) to membrane proteins and as evidenced by Potgens et al the anti-PS antibodies taught by Huppertz et al do not just bind phospholipid alone, but require a protein cofactor to bind efficiently to phospholipids such as PS (i.e., epitopes formed by the association of substances from different classes of substances; proteolipids). Finally, in response to applicant's arguments against the references individually (i.e., Huppertz et al reference), one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

The response also argues that a combination of Huppertz with any of the other cited references would not have led to the process of the present claims. In response to applicant's arguments that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art.

See In re Fine 5 USPQ2d 1596 (Fed. Cir 1988) and In re Jones 21 USPQ2d 1941 (Fed. Cir. 1992). In this case the teachings of Schroit A. J. pertaining to the need for an effective method of producing highly-specific anti-PS antibodies for use in the diagnosis and treatment of various cancers and the inherent problems with lipid immunogenicity and cross-reactivity (i.e., conserved epitopes) (see column 21, lines 17-28) and the teachings of Michael et al indicating success in producing monoclonal antibodies against mammalian antigens with highly conserved epitopes such as phospholipids and carbohydrates by immunizing a non-mammal with mammalian antigens/epitopes and immortalizing the immune response to obtain a phage library of antibodies and the teachings of Huppertz et al that blockage of PS by antibodies inhibit syncytium formation (i.e., syncytial cell-cell fusion as discussed above) in choriocarcinoma and primary trophoblast cells would have led one of ordinary skill in the art at the time the invention was made to adopt the method of Michael et al to solve the inherent problems with lipid immunogenicity and cross-reactivity for making a phage library of anti-PS antibodies, wherein the antibodies are useful for treating cancer and for preventing pregnancy by inhibiting syncytial cell-cell fusion (syncytium formation) as taught by Schroit et al and Huppertz et al. The strongest rationale for combining reference is a recognition, expressly or implicitly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent that some advantage or expected beneficial result would have been produced by their combination In re Sernaker 17 USPQ 1, 5-6 (Fed. Cir. 1983) see MPEP 2144.

*New Grounds of Rejections*

15. Claim 20 is objected to because of the following informalities:

Claim 20 recites "association of submits" which appears to be intended to recite "association of subunits".

Appropriate correction is required.

16. Claim 22 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 22 is indefinite for reciting "expressed on the surface" because the surface on which the mammalian epitopes are expressed is not defined. What surface are the mammalian epitopes expressed?

***Conclusions***

17. No claim is allowed.

18. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached at (571) 272-0787. The official fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,
David J. Blanchard
571-272-0827

LARRY R. HELMS, PH.D
PRIMARY EXAMINER